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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/647,695	04/06/2001	Sean Farmer	19374-502	1128

7590 05/31/2002
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EXAMINER

DAVIS, RUTH A

ART UNIT	PAPER NUMBER
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1651

DATE MAILED: 05/31/2002

12

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/647,695

Applicant(s)

FARMER ET AL.

Examiner

Ruth A. Davis

Art Unit

1651

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 06 March 2002.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-4 and 8-77 is/are pending in the application.
- 4a) Of the above claim(s) 31-76 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-4, 8-30, 77 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____
- 4) ☐ Interview Summary (PTO-413) Paper No(s) _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____

DETAILED ACTION

Applicant's amendment has been received and entered into the case. Claims 5 – 7 have been cancelled and claim 77 has been added. Claims 31 – 76 have been withdrawn from consideration, claims 1 – 4, 8 – 30 and 77 have been considered on the merits. All arguments have been fully considered.

Claim Objections

1. Claims 1, 12, 24, 27 and 77 are objected to because of the following informalities:

In claims 1 and 77, line 2, "effectic" should be spelled "effective".

In claim 12, line 2, "ofrom" should be spelled "from".

In claim 24, line 2, "gembibrozil" should be spelled "gemfibrozil" and "fenobibrate" should be spelled "fenofibrate".

In claim 27, line 1, "siad" should be spelled "said".

Appropriate correction is required.

Claim Rejections - 35 USC § 112

2. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Art Unit: 1651

3. Claims 2 – 3 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 2 – 3 are drawn to a method for decreasing serum cholesterol, however are rendered vague and indefinite because it is unclear how a lactic acid bacteria *B. coagulans* can further be any member of *Bacillus*, *Lactobacillus*, *Sporolactobacillus* and *Bifidobacterium*. Moreover, the claims appear to include both a narrow range and a broad range limitation.

Claim Rejections - 35 USC § 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

5. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Art Unit: 1651

6. Claims 1 – 4, 8 – 30 and 77 are rejected under 35 U.S.C. 103(a) as being unpatentable over Paul (US 5531989) in view of Fukushima (1995), Bova (2001/0006644) and Mandeville (US 5607669).

Applicant claims a method for decreasing serum cholesterol and increasing serum HDL comprising orally administering an effective amount of a composition comprising *Bacillus coagulans* and a therapeutic composition selected from a cholesterol reducing agent or a bifidogenic oligosaccharide. The composition contains 10^5 – 10^{10} viable bacterium/gram composition. Administration is oral at 0.1 – 5 grams/day, 10^8 – 10^{10} viable bacterium per day or 5×10^8 – 10^9 viable bacterium/day. Administration is 10 mg – 20 or 150 mg – 5 grams of bifidogenic oligosaccharide per day. The bifidogenic oligosaccharide is selected from fructo-oligosaccharide, gluco-oligosaccharide or trisaccharide raffinose wherein fructose-oligosaccharide comprises polymers of fructose and glucose with a chain length of about 4 – 100 sugar units. The composition comprises 10 mg – 1 gram or 100 – 500 mg of bifidogenic oligosaccharide per gram composition. The cholesterol reducing agent is one of a statin, a bile sequestering compound, a fiber product capable of binding cholesterol, niacin or aspirin. The statin is one of cervastatin, fluvastatin, lovastatin, pravastatin or simvastatin and is administered at 10 – 80 mg of statin per day, The bile sequestering agent is one of colestipol or cholestyramine and is administered at 1 – 20 grams per day. The fiber is one of gemfibrozil, fenofibrate, psyllium bran, glucomannan or Jerusalem artichoke flour and is administered at 500 mg – 50 grams of fiber per day. The composition further comprises a cholic acid complexation agent selected from a metal salt of calcium, chromium copper, iodine, iron, magnesium, manganese, potassium, sodium or zinc. The metal salt is calcium citrate, potassium gluconate, magnesium

Art Unit: 1651

citrate or chromium picollinate. The composition further comprises a food substance, flavoring, vitamin or mineral. Further, the patient is at risk for atherosclerosis, arterial sclerosis, myocardial infarction, heart attack, diabetes, coronary heart disease, angina pectoris or unstable angina. Finally, Applicant claims a method for decreasing serum cholesterol and increasing serum HDL comprising orally administering an effective amount of a composition comprising *Sporolactobacillus*, or *S. P44*, and a therapeutic composition selected from a cholesterol reducing agent or a bifidogenic oligosaccharide.

Paul teaches oral administration of a composition comprising dietary fiber (cholesterol reducing agent), fructooligosaccharide (FOS), and a beneficial human intestinal microorganism (lactic acid bacteria) wherein the microorganism is *Lactobacillus* or *Bifidobacteria* (abstract). Specific lactic acid microorganisms are disclosed to include *L. acidophilus*, *L. casei*, *L. salivarius*, *L. brevis*, *L. plantarum*, *B. adolescentis*, *B. infantis*, *B. longum* and *B. bifidum* (col.4 line 20-30).

The ingredients are combined with juice or water and are taken in dosages of about 20 – 400 mg/kg body weight (col.14 line 5-10). Paul discloses compositions such as this have beneficial effects on cholesterol metabolism resulting in decreased serum cholesterol and increased HDL to LDL ratio (col.2 line 35-40). Specifically, FOS is disclosed to reduce serum cholesterol, improve HDL/LDL ratios and increase bifidobacterium populations (col.6 line 55-68).

Although Paul does not specifically teach administering the composition in a method to decrease serum cholesterol and increase serum HDL, the reference does teach these effects. Furthermore, by administering the composition of Paul, it is inherent that serum cholesterol

Art Unit: 1651

decreased and serum HDL increased. Moreover, by practicing the method of Paul, one in the art would inherently be decreasing serum cholesterol and increasing serum HDL.

Paul does not teach the specific amounts of viable microorganisms of bacterium or bifidogenic oligosaccharide per gram of composition or the administration dosages as claimed by applicant. However, it would have been obvious to one of ordinary skill in the art to optimize volumes of ingredients and effective amounts of bacterium because it was routine practice in the art at the time of the invention. At the time of the invention, one of ordinary skill in the art would have been motivated by Paul to optimize the effective amounts to reduce serum cholesterol and increase serum HDL because of these disclosed known actions of the composition. Moreover, at the time of the invention, one of ordinary skill in the art would have been motivated by Paul and conventional practice to optimize administration dosages and volumes of ingredients with a reasonable expectation of success to reduce serum cholesterol and increase serum HDL.

Paul does not teach the fructooligosaccharide with a chain length of 4 – 100 sugar units. However, at the time of the invention, it would have been obvious to one of ordinary skill in the art to substitute or optimize the size of fructooligosaccharide to enhance a desired effect because it was routine practice in the art at the time of the invention. Moreover, at the time of the invention, one of ordinary skill in the art would have been motivated by conventional practice to optimize the size of the fructooligosaccharide in the method of Paul, with a reasonable expectation of success for decreasing serum cholesterol and increasing serum HDL.

Paul does not teach Jerusalem artichoke flour as the fiber source. However, Paul does teach inulin as the fiber source (abstract). Specifically, Paul teaches Jerusalem artichoke is a rich

Art Unit: 1651

source of inulin (fiber) wherein Bifidobacterium uses it as an energy source (col. 6 line 5-20). At the time of the invention, one of ordinary skill in the art would have been motivated to use Jerusalem artichoke flour because of the fiber (inulin) content contained in Jerusalem artichoke as taught by Paul. One of ordinary skill in the art would have been further motivated to use Jerusalem artichoke flour because it was known to be a source of energy for Bifidobacterium as disclosed by Paul.

Paul does not teach the method wherein the patient is at risk for atherosclerosis, arterial sclerosis, myocardial infarction, heart attack, diabetes, coronary heart disease, angina pectoris or unstable angina. However, because of the disclosed beneficial effects on serum cholesterol and LDL/HDL ratios, it would have been obvious to one of ordinary skill in the art to practice the method of Paul on patients at risk for the aforementioned conditions because high cholesterol was a known symptom/indicator of each of the conditions. Moreover, at the time of the invention, one of ordinary skill in the art would have been motivated to practice the method of Paul on "at risk patients" with a reasonable expectation for success because of the disclosed benefits of reduced serum cholesterol and improved LDL/HDL ratios.

Paul does not teach the method wherein Bacillus species are used. However, at the time of the invention, it would have been obvious to one of ordinary skill in the art to utilize a Bacillus in the methods of Paul because Fukushima teaches the effects of a probiotic composed of Bacillus include reduced serum cholesterol and increased serum HDL (abstract). Although Fukushima does not teach specific species of Bacillus, the reference does teach the effect is achieved with the genus. Therefore, at the time of the invention, it would have been obvious to one of ordinary skill in the art to utilize any Bacillus as they were known to have the claimed

Art Unit: 1651

effect. Moreover, at the time of the invention, one of ordinary skill in the art would have been motivated by Fukushima to use a Bacillus in the methods of Paul with a reasonable expectation for success of decreasing serum cholesterol and increasing serum HDL because of the disclosed properties of Bacillus specifically achieving the claimed effect.

Paul does not teach the method wherein therapeutic agents include statins, cervastatin, flucastatin, lovastatin, pravastatin or simvastatin; bile sequestering agents, colestipol or cholestyramine; fiber sources gemfibrozil or fenofibrate; niacin or aspirin wherein they are administered in amounts as claimed by applicant. However, at the time of the invention, one of ordinary skill in the art would have been motivated to include any of the aforementioned agents in the composition and method of Paul because Bova teaches each of these are known to lower serum cholesterol (p.1, paragraphs 0006 – p.2 paragraph 0009). Bova teaches numerous methods for reducing serum cholesterol and increasing HDL cholesterol levels have been proposed to include administration of hypolipidemic agents, or lipid altering agents (p.1 paragraph 0006). Specifically, niacin and the named statins are disclosed to reduce total serum cholesterol and increase serum HDL cholesterol (p.2 paragraph 0010, 0017) while bile sequestering agents are disclosed to be a first choice for treating hypercholesterolemia due to their efficacy and proved usefulness (p.3 paragraph 0020). Furthermore, Bova teaches administration of statins in dosages between 10 – 80 mg, 5 – 80 mg and 20 – 80 mg (p.4 paragraph 0033). Therefore, at the time of the invention, one of ordinary skill in the art would have been motivated by Bova to include any of the above mentioned agents in the method of Paul, with a reasonable expectation of success for decreasing serum cholesterol and increasing

Art Unit: 1651

serum HDL because they were well known in the art for reducing cholesterol and increasing HDL as demonstrated by the references cited above.

The above references do not teach specific volumes of bile sequestering agents or fiber. However, at the time of the invention, it would have been obvious to one of ordinary skill in the art to optimize dosages of effective ingredients because it was routine practice in the art at the time of the invention. Moreover, at the time of the invention, one of ordinary skill in the art would have been motivated by conventional practice to optimize dosages of effective ingredients with a reasonable expectation of success for decreasing serum cholesterol and increasing serum HDL.

Paul does not teach the method further comprising administering a cholic acid complexation agent. However, at the time of the invention, one of ordinary skill in the art would have been motivated to include a cholic acid complexation (or sequestering, chelating) agent because Mandeville teaches that it is advantageous to sequester primary bile acids to significantly increase the reduction of serum lipid levels (col.1 line 55-65). At the time of the invention, it was known in the art that cholic acid is a primary bile acid and that sorption of bile acids is related to decreasing serum cholesterol (US 5427777 col.2 line 25-35). Although the reference does not teach the specific cholic acid complexation (sequestering) agents claimed by applicant, it would have been obvious to one of ordinary skill in the art to use any complexing agent as they were known in the art at the time of the invention. Moreover, at the time of the invention, one of ordinary skill in the art would have been motivated by Mandeville to include a cholic acid complexation (sequestering) agent in the method of Paul with a reasonable

Art Unit: 1651

expectation of success for reducing serum cholesterol because of the cholesterol/lipid reducing effects as demonstrated by Mandeville.

Applicant argues that the references do not teach *Bacillus coagulans* in methods for reducing serum cholesterol and that there is no suggestion or motivation to use the particular claimed species of *Bacillus* in the methods of Paul.

However, these arguments fail to persuade, because as clearly demonstrated by the cited references, it was well known in the art that lactic acid bacteria were well known to reduce serum cholesterol levels and increase serum HDL. Although the references do not name the specifically claimed species, it would have been obvious to one of ordinary skill in the art to use any known lactic acid bacteria because they were well known to have the beneficial effects, as claimed.

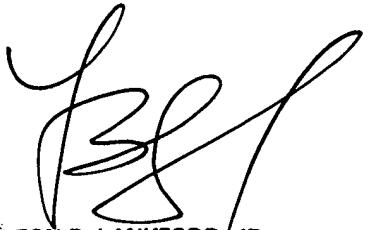
Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ruth A. Davis whose telephone number is 703-308-6310. The examiner can normally be reached on M-H (7:00-4:30); altn. F (7:00-3:30).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn can be reached on 703-308-4743. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4242 for regular communications and 703-308-4242 for After Final communications.

Art Unit: 1651

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Ruth A. Davis; rad
May 29, 2002



LEON B. LANKFORD, JR.
PRIMARY EXAMINER